ECHA
EUROPEAN CHEMICALS AGENCY

Decision number: CCH-D-0000002979-55-03/F Helsinki, 19 September 2013

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For 1-nitroguanidine, CAS No 556-88-7 (EC No 209-143-5), registration number: [redacted]

Addressee: [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration dossier for 1-nitroguanidine, CAS No 556-88-7 (EC No 209-143-5), submitted by [redacted] (Registrant). The scope of this compliance check is limited to the standard information requirements of Annex VII, Sections 7.8. and 8.4., and Annex VIII, Section 8.4. of the REACH Regulation.

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 1000 tonnes or more per year. This decision does not take into account any updates after 20 June 2013, the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

This compliance check decision does not prevent ECHA from initiating further compliance checks on the present dossier at a later stage.

The compliance check was initiated on 21 September 2012.

On 14 December 2012 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

By 14 January 2013 the Registrant did not provide any comments on the draft decision to ECHA.

On 20 June 2013 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals to amend the draft decision within 30 days of the receipt of the notification.

Subsequently, Competent Authorities of the Member States did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

II. Information required

Pursuant to Articles 41(1)(a) and (b), 41(3), 10(a)(vi), 12(1)(e), 13 and Annexes VII and VIII of the REACH Regulation the Registrant shall submit the following information for the registered substance subject to the present decision:

1. Partition coefficient n-octanol/water (Annex VII, 7.8.) determined by using an appropriate test method;
2. *In vitro* cytogenicity study in mammalian cells (Annex VIII, 8.4.2., test method: EU B.10/ OECD 473) or *in vitro* micronucleus study (Annex VIII, 8.4.2.; test method: OECD 487).

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated IUCLID dossier to ECHA by **19 September 2014**.

Guidance for determining appropriate test methods for the partition coefficient n-octanol/water is available in ECHA's Guidance on information requirements and chemical safety assessment, Chapter R.7(a), section R.7.1.8.3. (pages 101 to 103, Version of May 2008).

III. Statement of reasons

Pursuant to Article 41(3) of the REACH Regulation, ECHA may require the Registrant to submit any information needed to bring the registration into compliance with the relevant information requirement. The scope of the present decision includes the partition coefficient n-octanol/water (Annex VII, 7.8. of the REACH Regulation) and the *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study (Annex VIII, 8.4.2. of the REACH Regulation). In accordance with Articles 10(a)(vi) and 12(1)(e) of the REACH Regulation, any registration for a substance manufactured or imported by a registrant at the tonnage level of 1000 tonnes or more per year shall contain this information.

1. Partition coefficient

The technical dossier contains data for this standard information requirement, which according to the information provided by the Registrant meets Klimisch criterion 4 only. In accordance with ECHA's Guidance on information requirements and chemical safety assessment, Chapter R.7(a)), section R.7.1.1.3 (page 33, Version of May 2008) test results that meet Klimisch criterion 3 or 4 could be used in a weight of evidence approach. The Registrant has submitted a weight of evidence adaptation according to Annex XI, Section 1.2 for this endpoint, but failed to provide adequate and reliable documentation for the information used. The Registrant is therefore requested to determine the partition coefficient n-octanol/water using an appropriate test method on the registered substance and to submit the resulting data.

2. *In vitro* cytogenicity study or *in vitro* micronucleus study

The technical dossier contains an adaptation to this standard information requirement. Applying a weight-of-evidence approach, the Registrant has submitted a study summary of an *in vitro* mammalian chromosome aberration test (Ishidate, M. Jr; Odshima S. Mutation Research, 48 (1977) 331-354). The Registrant himself has classified the study as "not reliable" and "unacceptable". Furthermore, the Registrant has stated that (a) the "study does not satisfy the requirement for Test Guideline OECD 473 for in vitro cytogenetic

mutagenicity data", (b) the "study is poorly documented", (c) the "method was reported in low detail", (d) "only 100 metaphases were counted", (e) "no details on the test compound were provided", and (f) "no dose dependency was reported". Furthermore, ECHA notes that the study has not been performed according to an acceptable Test Guideline and that e.g. no metabolic activation was conducted. Therefore, the information does not fulfil the endpoint by itself. Furthermore, the Registrant submitted test results of a mouse lymphoma mutation assay and a sister chromatid exchange assay of nitroguanidine in chinese hamster ovary cells. These tests cannot by themselves fulfil the standard information requirement according to Annex VIII, 8.4.2, i.e. for *in vitro* cytogenetics. The Registrant has not provided any justification why the data from the supporting studies together with the unacceptable *in vitro* mammalian chromosome aberration test are sufficient weight of evidence for concluding on the endpoint in question and has therefore not succeeded in justifying a weight of evidence argument pursuant to Section 1.2. of Annex XI.

The endpoint has not been fulfilled and no valid adaptation was provided. Consequently there is an information gap and it is necessary to generate the data for this endpoint. Therefore, the Registrant is requested to submit the information for this endpoint using one of the abovementioned test methods on the registered substance.

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted for identifying the substance has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In carrying out the studies required by the present decision it is important to ensure that the particular sample of substance tested is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured. If the registration of the substance covers different grades, the sample used for the new studies must be suitable to assess these.

Furthermore, there must be adequate information on substance identity for the sample tested and the grade registered to enable the relevance of the studies to be assessed.

V. General requirements for the generation of information and Good Laboratory Practice

ECHA reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP).

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

VI. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on ECHA's internet page at http://echa.europa.eu/appeals/app_procedure_en.asp. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

[redacted]
Jukka Malm
Director of Regulatory Affairs